CLAIMS

What is claimed is:

Claim 1. The use of rotavirus protein VP4, its functional variants, derived proteins, derived fusion proteins and functional peptides derived from them as well as their mixtures, for the preparation of a pharmaceutical composition that allows the passage or enhance the delivery of pharmaceutical agents through the paracellular pathway.

Claim 2. The use as claimed in claim 1, wherein protein VP4 is SEQ. ID: No. 1.

Claim 3. The use as claimed in claim 1, wherein the derived functional peptide is VP8 (SEQ. ID: No. 2).

Claim 4. The use as claimed in claim 1, wherein the derived functional peptide of VP8 is SEQ. ID: No. 3.

Claim 5. The use as claimed in claim 1, wherein the derived functional peptides of VP8 is selected from the group consisting of: VVKT (SEQ. ID. NO. 4), SYSQYGPL (SEQ. ID. NO 5), IYTY (SEQ. ID. NO. 6) and NVTT (SEQ. ID. NO. 7).

Claim 6. The use of rotavirus protein VP4, its functional variants, derived proteins, derived fusion proteins and functional peptides derived from them as well as their mixtures, for the preparation of a pharmaceutical composition for the delivery of a therapeutic agent to a subject in need.

Claim 7. The use of antibodies, either monoclonals or polyclonals against proteins VP4, VP8 or their derived functional peptides, which are capable of exerting effects on the paracellular barrier as proteins VP4, VP8 or their functional derivatives.

Claim 8. A pharmaceutical composition for the delivery of a therapeutic agent comprising:

(A) a therapeutic agent; and

(B) an effective amount of protein VP4, VP8 its functional variants, derived proteins, derived fusion proteins and functional peptides derived from them as well as their mixtures.

(C) optionally an acceptable pharmaceutical vehicle.

Claim 9. A pharmaceutical composition as claimed in claim 8, wherein said composition is an oral dosage composition for intestinal delivery of a therapeutic agent, and administering is by oral administration.

Claim 10. A pharmaceutical composition as claimed in claim 8, wherein said composition is a nasal dosage composition for administering by nasal administration.

Claim 11. A pharmaceutical composition as claimed in claim 8, wherein said composition is a cutaneous dosage composition for administering by the skin.

Claim 12. A pharmaceutical composition as claimed in claim 8, wherein said composition is a vaginal dosage composition for administering by the vagina.

Claim 13. A pharmaceutical composition as claimed in claim 8, wherein said composition is a rectal dosage composition for administering by the rectum.

Claim 14. A pharmaceutical composition as claimed in claim 8, wherein said composition is in the form of an aerosol dosage composition for administering to the respiratory system.

Claim 15. A pharmaceutical composition as claimed in claim 8, wherein said composition is an intravenous dosage composition for delivery of said therapeutic agent through the blood-brain barrier, and said administering is by intravenous

administration.

Claim 16. The therapeutic agent employed as claimed in claim 8, can be any drug, peptide with biological activity, vaccine, or any composition that is not adequately absorbed by the transcellular route, without taking into account its size or charge.

Claim 17. The drugs employed as claimed in claim 16, are those that act on the cardiovascular system, the central nervous system, antineoplastic drugs and antibiotics.

Claim 18. The pharmaceutical composition of claim 17, wherein said drug which acts on the cardiovascular system is selected from the group consisting of lidocaine, adenosine, dobutamine, dopamine, epinephrine, norepinephrine and phentolamine.

Claim 19. The pharmaceutical composition of claim 17 wherein said drug which acts on the central nervous system is selected from the group consisting of doxapram, alfentanil, dezocin, nalbuphine, buprenorphine, naloxone, ketorolac, midazolam, propofol, metacurine, mivacurium and succinylcholine.

Claim 20. The pharmaceutical composition of claim 17, wherein said antineoplastic drug is selected from the group consisting of cytarabine, mitomycin, doxorubicin, vincristine and vinblastine.

Claim 21. The pharmaceutical composition of claim 17, wherein said antibiotic is selected from the group consisting of methicillin, mezlocillin, piperacillin, cetoxitin, cefonicid, cefmetazole and aztreonam

Claim 22. The pharmaceutical composition of claim 16, wherein said biologically active peptide is selected from the group consisting of a hormone, lymphokine, globulin and albumin.

Claim 23. The pharmaceutical composition of claim 22, wherein said hormone is selected from the group consisting of testosterone, nandrolene, menotropins, insulin and urofolltropin.

Claim 24. The pharmaceutical composition of claim 22, wherein said lymphokine is selected from the group consisting of interferon-alpha, interferon-beta, interferon-gamma, interleukin-1, interleukin-2, interleukin-4 and interleukin-8.

Claim 25. The pharmaceutical composition of claim 22, wherein said globulin is selected from the group consisting of alpha-globulins, beta-globulins and immunoglobulins.

Claim 26. The pharmaceutical composition of claim 22, wherein said globulin is an immunoglobulin selected from the group consisting of polyvalent IgG, and specific IgG, IgA or IgM.

Claim 27. The pharmaceutical composition of claim 22, wherein said albumins is selected from the group consisting of human seric albumin and ovalbumin.

Claim 28. The pharmaceutical composition of claim 16, wherein said vaccine is selected from the group consisting of viral peptidic antigens, attenuated microorganisms, as well as vaccines based in RNA replicons, small interfering RNAs (siRNAs), virus like particles (VLPs), subunit virus vaccines, DNA and RNA vaccines.

Claim 29. The pharmaceutical composition of claim 28, wherein said peptidic antigen include the B subunit of the heat sensitive enterotoxin of enterotoxic E. coli, the B subunit of cholera toxin, capsular antigens of enteric pathogens, fimbria and pili of enteric pathogens, surface antigens of HIV, dust allergens and acarus.

Claim 30. The pharmaceutical composition of claim 28, wherein said

attenuated microorganisms include those of enterotoxic E. coli, enteropathogen E. coli, enterohemorragic E.coli, enteroinvasive E. coli, Vibrio Cholera, Shigella flexneri, Salmonella typhy, Helicobacter pylori, rotavirus, astrovirus, adenovirus and calicivirus.

Claim 31. The pharmaceutical composition of claim 8, wherein said the therapeutic agent is insulin.

Claim 32. A method for treating diabetes comprising orally administering, to a diabetic subject, an oral dosage composition for intestinal delivery of a therapeutic agent comprising:
(A) a therapeutically effective amount of insulin; and
(B) an intestinal absorption enhancing effective amount of of rotavirus protein VP4, its functional variants, derived proteins, derived fusion proteins and functional peptides derived from them as well as their mixtures.

Claim 33. A method for the treatment of cancer comprising the administering by any route, to a cancerous subject, rotavirus protein VP4, its functional variants, derived proteins, derived fusion proteins and functional peptides derived from them as well as their mixtures, together with an acceptable pharmaceutical vehicle.

Claim 34. A method for treating cancer in mammals, where epithelial transformation is related to over expression of tight junction proteins, comprising the administering by any route, of rotavirus protein VP4, its functional variants, derived proteins, derived fusion proteins and functional peptides derived from them as well as their mixtures.

Claim 35. A method to treat cancer and/or inhibit metastasis, by disrupting the growth of new capillaries comprising the administering by any route, of rotavirus protein VP4, its functional variants, derived proteins, derived fusion proteins and functional peptides derived from them as well as their mixtures.

Claim 36. A method to reduce unwanted cellular adhesion that can occur between tumor cells or normal cells, as a result of surgery, injury, chemotherapy, disease, inflammation or other pathological condition, comprising the administering by any route, of rotavirus protein VP4, its functional variants, derived proteins, derived fusion proteins and functional peptides derived from them as well as their mixtures.

Claim 37. A method for determining the regions or the derived peptides of proteins VP4, VP8 or of their functional variants and fusion proteins, that enhance or modulate the opening of the paracellular pathway, comprising:

A) culture, extraction or isolation of an epithelia or endothelia;

B) determination of the transepithelial electrical resistance (TER) of such tissue;

C) addition of peptides, fragments, fusion proteins or functional derivatives of proteins VP4 and VP8;

D) optionally a molecule or compound unable to cross a sealed paracellular pathway could be added;

E) Identification of the proteins and peptides derived from proteins VP4 and VP8, or of their mixtures, that have been able to diminish the TER of the tissue or that have allowed the passage of a paracellular tracer molecule.

Claim 38. An isolated peptide with SEQ. ID. NO. 3

Claim 39. An isolated peptide with SEQ. ID. NO. 4

Claim 40. An isolated peptide with SEQ. ID. NO. 5

Claim 41. An isolated peptide with SEQ. ID. NO. 6

Claim 42. A peptide with SEQ. ID. NO. 7